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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/961,028	09/21/2001	Donghao Robert Lu	G25-065	4699

7590 06/16/2004

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/961,028	LU ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

eriod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

tatus

1)☒ Responsive to communication(s) filed on *25 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

isposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *18-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

\pplication Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

riority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

ttachment(s)

☒ Notice of References Cited (PTO-892)
☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEGMENT TO RESTRICTION REQUIREMENT, IDS AND STATUS OF THE CLAIMS

1. The information disclosure statements (IDS) and Forms PTO-1449 filed 9/13/02 and the response to the restriction requirement filed 3/25/04 are acknowledged, entered and considered. Claims 1-33 are now pending in the application.

ELECTION WITH TRAVERSE

2. Applicant's election with traverse of Group I (claims 1-17 and 33) in Paper No. 5 is acknowledged. The traversal presented in the election has been considered persuasive for the reasons set forth in the traverse with respect to the composition claims of Group I since the compositions are conceptually related and are all pharmaceutical compositions. Hence, the Office action is directed to the merits of claims 1-17 and 33 as elected invention and the previous requirement for election of species has been withdrawn. However, claims 18-32 are withdrawn from consideration as non-elected invention.

OBJECTION TO THE SPECIFICATION, CLAIMS AND ABSTRACT

3. The specification, claims, abstract and the Figures are objected in the recitation "EL 890 534 405 US" at the front corner of each page of the specification, claims and abstract. Also, the specification, claims, abstract and Figures are objected in the

recitation "09/21/2001" at the end corner of the specification, claims, abstract and Figures. Deletion of the above file locator from the disclosure of the specification, claims, abstract and Figures would obviate this objection. Further, there are no descriptions for the drawings of Figures 1-5 disclosed in the specification, except for the recitation on page 12, line 31 "See attached figure 4" and on page 15, line 14 "See attached Figure 3", respectively. Appropriate correction is required.

CLAIMS REJECTION-35 U.S.C. § 112^{2nd} PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-17 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 33 are indefinite in the recitation "optionally" because if an ingredient, a step or other structural element is truly optional, i.e., its presence is not necessary for attainment of the result that is an object of the invention, and then, recitation thereof does not belong in the claims.

Regarding claims 3, 7 and 9, the phrase "such as" render the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 4 recites the limitation "said phospholipid" in line 1. There is insufficient antecedent basis for this limitation in claim 4 or 1.

Claims 4, 10, 14, 16 and 33 are indefinite in the recitation "and mixtures, thereof" because it is unclear as to what are the mixtures; amounts of the components in the mixtures; and which components? Appropriate clarification is required especially as to what is the increased concentration.

Regarding claim 7, the phrases "for example" (i.e., e.g.,) renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 7 is in the recitation "and/or" because it is not clear whether "and" or is it "or" is claim meant in the conjunctive or is the "/" meant used in the alternative. Appropriate clarification is required.

Claim 7 is indefinite and confusing in referring back or incorporating as a reference a U.S. Patent No. 4,689,338 because referring back to a reference or a Figure or a Table is not acceptable claim language. Such material should be incorporated within the claim language. Further, the claims should be complete and self-contained and incorporation into claims by express reference to the specification or patent is not permitted and should not be relied on to define the invention (ex parte Fressola, Bd. Pat. Appl. & Inter., 5/11/93, p.1608).

Claim 7 is indefinite in the recitation "and the like" and "as well as" because the phrases "and the like" and "as well as" appear to be superfluous in the claim as they do not serve to define and/or limit the composition of the bioactive agent claimed. Deletion of these phrases is suggested as it would not affect the scope of the claim.

Claim 7 is indefinite and confusing in the recitation "clathrates thereof" because it is not clear what is the clathrate? Appropriate clarification is required.

Claim 8 is indefinite in the recitation "(like bacterial invasions)" because the phrase "(like bacterial invasions)" appears to be superfluous in the claim as it does not serve to define and/or limit the composition of the bioinvasive molecules claimed. Deletion of this phrase is suggested as it would not affect the scope of the claim.

Claim 16 recites the limitation "said triglycides" in line 1. There is insufficient antecedent basis for this limitation in claim 16 or 1.

CLAIM REJECTION-35 U.S.C. § 102(b)

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-10 11, 17 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 93/20800).

WO 93/20800 discloses a pharmaceutical composition comprising a microemulsion which contains a bioactive agent for drug delivery, liposomes wherein the bioactive agent incorporated a) a core surrounded by a bilayer of a lipid substance, typically a phospholipid (together with e.g., cholesterol which is steroid and sphingomyelin), or b) if desired therapeutic compound is amphiphilic (e.g., an anti-cancer phospholipid, it is incorporated in the bilayer itself, fro example, an emulsion of

bioactive agent, such as a lipohphilic drug surrounded by a monolayer of phosphatidyl choline, are used. The pharmaceutical composition is preferably an aqueous solution for parenteral use, such as for injection purpose (e.g., i/v), containing a therapeutically or diagnostically effective amount bioactive agent containing carrier particles together with amphipathic lipid. The ratio (weight) of carrier particles to amphipathic lipid ranges 2 to 40% by weight of said composition, which overlaps the claimed amount ranging from about 0.01% to about 60% by weight of the composition or about 0.05% to about 25% by weight of steroidal component as claimed I claims 1 and 5 (See e.g. pages 3-6 and the Example) as directed to claims 1-2, 4-10 and 33 . On page 2, lines 11 to 14, the reference discloses cells containing on their surfaces specific LDL-receptors which bind to the LDL-particle by specifically recognizing the protein component of the LDL-surface, I.e., apolipoprotein B. Thus, teaching the use of lipidized protein, which is apolipoprotein B, and as such meet the limitation of claim 11. The prior art discloses the use of a composition diagnostic or therapeutic purpose containing a bioactive agent, which is boronated fatty acid ester (See e.g., page 8, lines 1-10) as directed to claim 17. Therefore, in the absence of evidence to the contrary or specific structural limitations, the prior art anticipates the claimed pharmaceutical compositions comprising a microemulsion as a carrier for a bioactive agent as drafted in claims 1-2, 4-10, 11, 17 and 33.

CLAIMS REJECTION-35 U.S.C. § 103(a)

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-17 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/20800 taken with Wretlind et al. (U.S. Patent No. 4,168,308).

The reference of WO 93/20800 as discussed above under the rejection 102(b) discloses a pharmaceutical composition comprising a microemulsion which contains a bioactive agent for drug delivery, liposomes wherein the bioactive agent incorporated a) a core surrounded by a bilayer of a lipid substance, typically a phospholipid (together with e.g., cholesterol which is steroid and sphingomyelin), or b) if desired therapeutic compound is amphiphilic (e.g., an anti-cancer phospholipid, it is incorporated in the bilayer itself, fro example, an emulsion of bioactive agent, such as a lipohphilic drug surrounded by a monolayer of phosphatidyl choline, are used. The pharmaceutical composition is preferably an aqueous solution for parenteral use, such as for injection purpose (e.g., i/v), containing a therapeutically or diagnostically effective amount

bioactive agent containing carrier particles together with amphipathic lipid. The ratio (weight) of carrier particles to amphipathic lipid ranges 2 to 40% by weight of said composition, which overlaps the claimed amount ranging from about 0.01% to about 60% by weight of the composition or about 0.05% to about 25% by weight of steroidal component as claimed I claims 1 and 5 (See e.g. pages 3-6 and the Example) as directed to claims 1-2, 4-10 and 33 . On page 2, lines 11 to 14, the reference discloses cells containing on their surfaces specific LDL-receptors which bind to the LDL-particle by specifically recognizing the protein component of the LDL-surface, I.e., apolipoprotein B. Thus, teaching the use of lipidized protein, which is apolipoprotein B, and as such meet the limitation of claim 11. The prior art discloses the use of a composition diagnostic or therapeutic purpose containing a bioactive agent, which is boronated fatty acid ester (See e.g., page 8, lines 1-10) as directed to claim 17.

The reference of WO 93/20800 differs from claims 1-17 and 33 in not teaching a) the use of chemically modified or conjugate phospholipid to increase the stability of the composition and the use of triglycerides which are vegetable oils to stabilize an amphipathic lipid. However, the secondary reference of Wretlind et al. on column 4, lines 62 to column 5, lines 3, states that in the vehicle systems most commonly used, which consists of an emulsion or suspension of a pharmacologically inert oil or fat in aqueous solution, the hydrophobic component usually consists of a fat or an oil of vegetable or animal origin, such as soybean oil, cotton seed oil, coconut oil or olive oil. In order to obtain a stable system, it is furthermore necessary to include stabilizers of a natural or synthetic origin, such as phosphatides, polypropylene glycol, polyethylene glycol, polyglycerol monoleate, etc. Thus, the prior art clearly teaches the use of chemically modified or conjugated phospholipid such as pegylated phospholipid as well

as the use of triglycerides, which are vegetable oils to stabilize the phospholipid (i.e., amphipathic lipid).

Therefore, in view of the above and in view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated at he time the invention was made to employ pharmaceutical compositions comprising a microemulsion which contains a bioactive agent, said microemulsion comprising a lipid core such as triglyceride which is stabilized by a monolayer of an amphipathic lipid, preferably a phospholipid and at least one bioactive agent may be dissolved or dispersed with the lipid core, the amphipathic lipid monolayer or, or even the surface of the microemulsion. Thus, claims 1-17 and 33 are *prima facie* obvious over the combined teachings of the prior art, absence of sufficient objective factual evidence or unexpected results to the contrary.

CONCLUSION AND FUTURE CORRESPONDENCE

7. Claims 1-17 and 33 are rejected and claims 18-32 are withdrawn from consideration as non-elected invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Mohamed/AAM

June 14, 2004